Noradrenergic dysfunction accelerates LPS-elicited inflammation-related ascending sequential neurodegeneration and deficits in non-motor/motor functions

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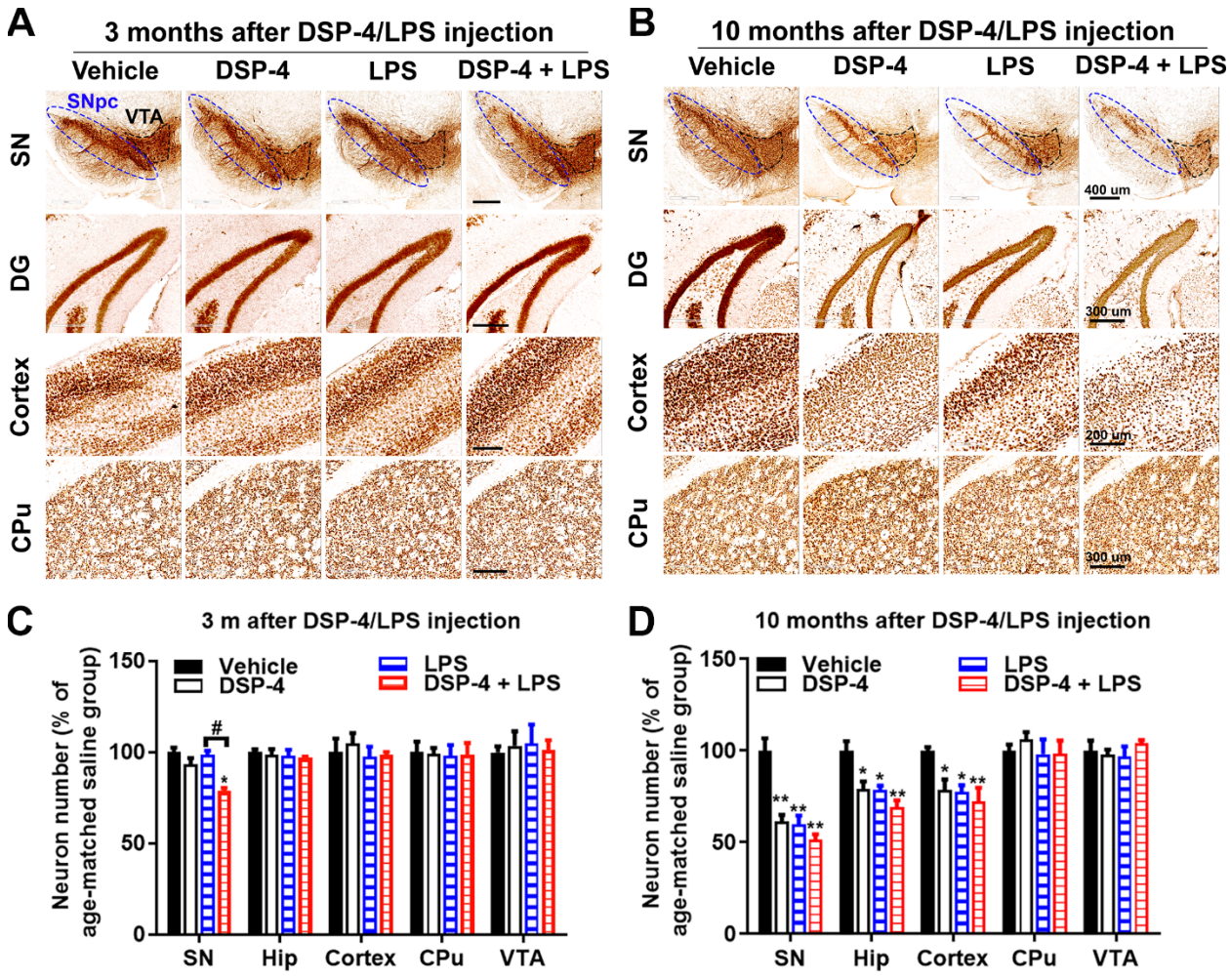
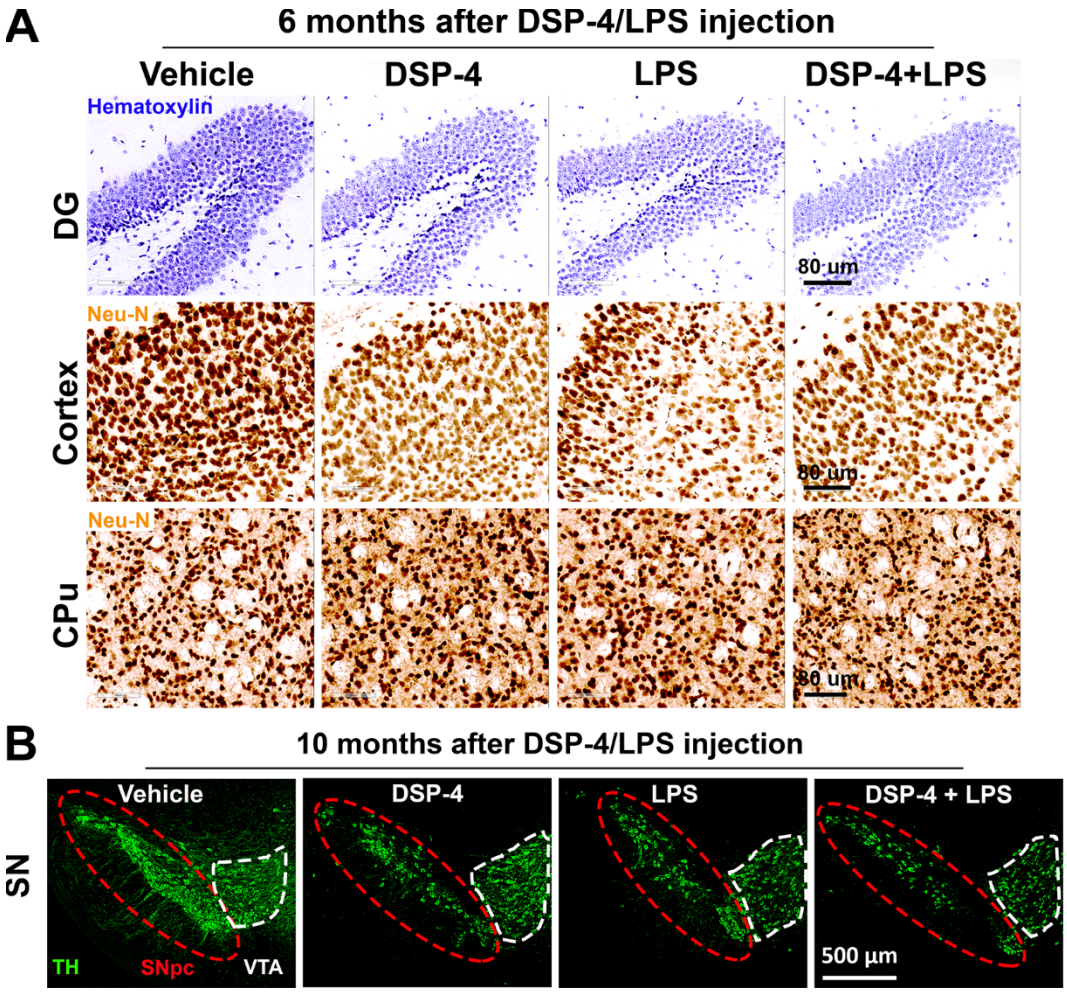
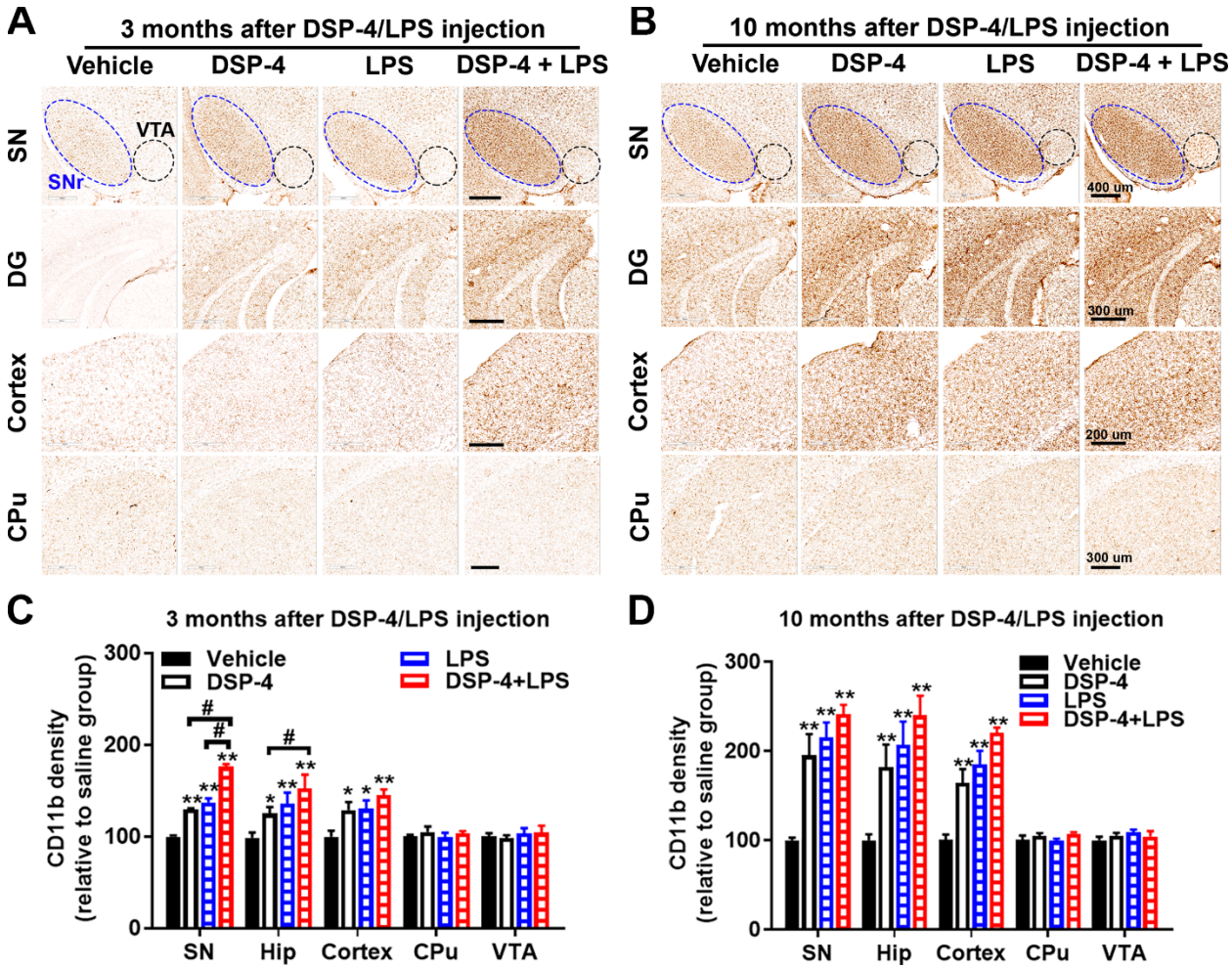
Supplementary Materials



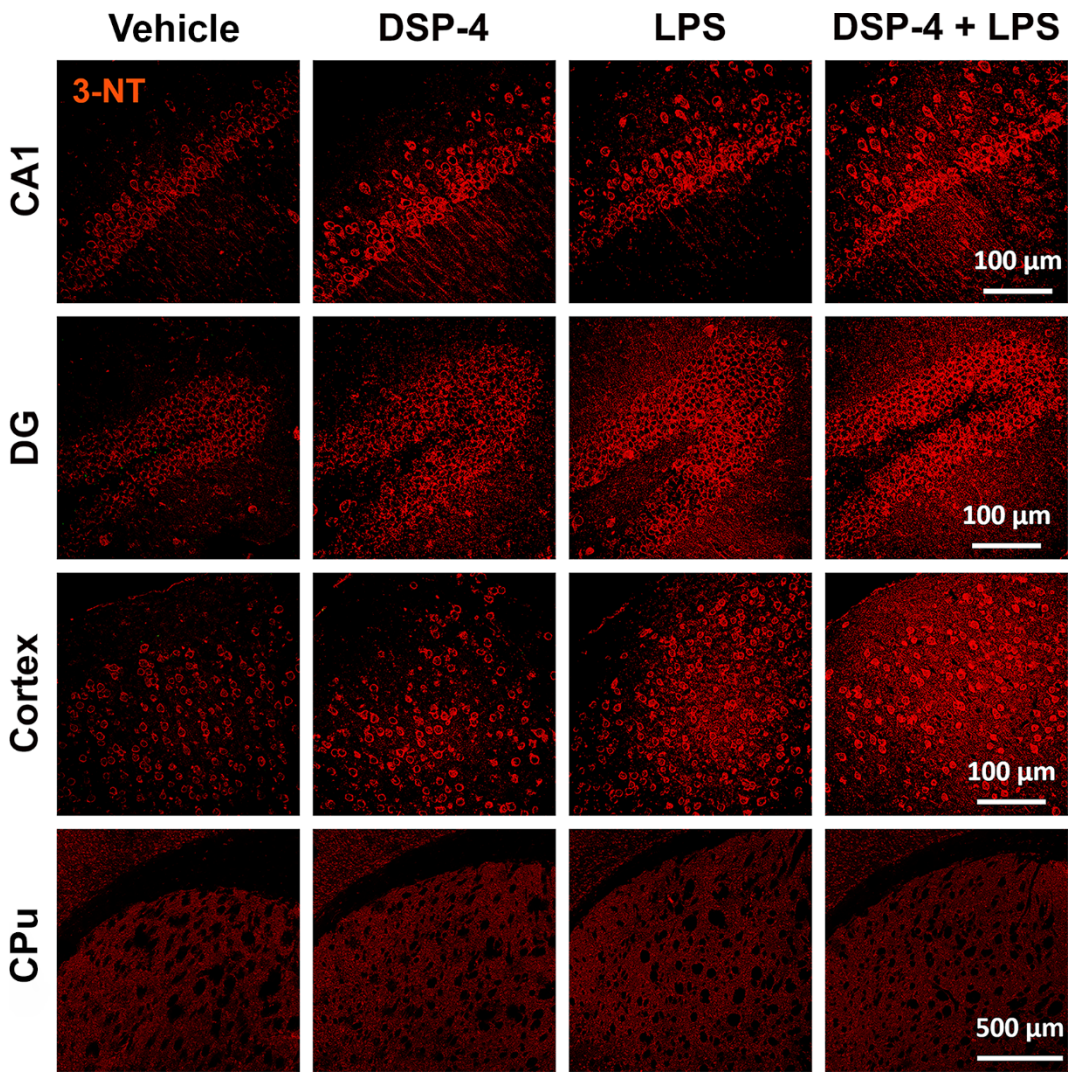
Supplementary Fig. 1. Representative images of staining in SN, hippocampus, cortex, and striatum at 3 (A) and 10 (B) months after DSP-4/LPS injection. Dopaminergic neurons in the SNpc were stained with anti-TH antibody. Neurons in hippocampal granule layer, cortex and striatum were stained with anti-Neu-N antibody. Scales as indicated in the pictures. (C, D) Quantitative analysis of neuron loss in the different brain regions at 3 (C) and 10 (D) months after DSP-4/LPS injection. Results are expressed as a percentage of age-matched vehicle controls (mean ± SEM) from 3-5 mice in each group at each time point. $^{*}p<0.05$ and $^{**}p<0.01$ compare with time-matched saline controls, $^{\#}p<0.05$ compare with indicated group.



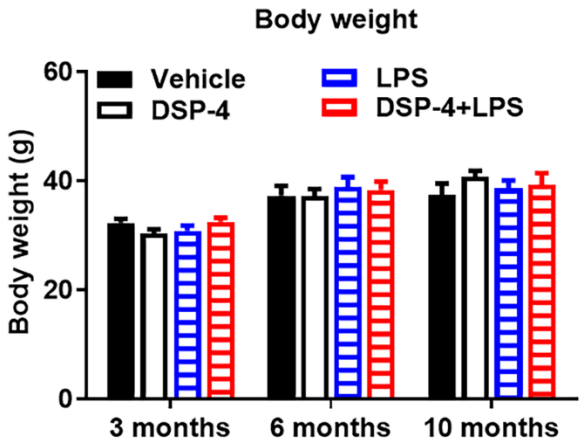
Supplementary Fig. 2. (A) High-power images show the changes of neuron number in hippocampus, cortex, and striatum at 6 months after injection. Neurons in hippocampal granule layer were labeled with hematoxylin; Neurons in cortex and striatum were stained with anti-Neu-N antibody. (B) High quality immunofluorescent images show the loss of TH^+ cell in SNpc rather than in VTA at 10 months after DSP-4/LPS injection. Scales as indicated in the pictures.



Supplementary Fig. 3. Representative images of CD11b staining in SN, VTA, hippocampus, cortex, and striatum at 3 (A) and 10 (B) months after DSP-4/LPS injection. Scales as indicated in the pictures. (C-D) Quantitative analysis of microglial activation in the different brain regions by measuring alterations of CD11b density at 3 (C) and 10 (D) months after DSP-4/LPS injection. Results are expressed as a percentage of age-matched vehicle controls (mean ± SEM) from 3-5 mice in each group at each time point. $^{*}p<0.05$ and $^{**}p<0.01$ compare with age-matched vehicle controls, $^{\#}p<0.05$ compare with indicated group.



Supplementary Fig. 4. Representative images show the increased oxidative stress (3-NT, red) in all those LC-innervated regions, including CA1, DG, and cortex after 6 months of DSP-4/LPS injection. Scales as indicated in the pictures.



Supplementary Fig. 5. There were no differences in body weight between treated groups vs. controls during these studies.

Supplementary Table 1. Lack of treatment effects on vision and swimming ability in the Morris water maze. Data are means (± SEM) of 4 trials per day.

	Vehicle	**DSP-4**	**LPS**	**DSP-4+LPS**
Visible platform, escape latency (s)				
Day 1	22 ± 4	25 ± 4	23 ± 4	26 ± 4
Day 2	8 ± 2	9 ± 2	15 ± 3	7 ± 1
Swim speed (cm/s)				
Day 1 of visible platform test	18 ± 0.3	19 ± 0.8	19 ± 0.5	18 ± 1.1
Day 1 of acquisition	20 ± 0.8	21 ± 0.5	20 ± 0.3	18 ± 0.9
Day 1 of reversal learning	18 ± 1.2	18 ± 1.2	18 ± 1.3	17 ± 1.3